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D14

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/181,585	10/28/98	RANUM L.	110.00900101

HM12/0403

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EXAMINER	
SOUAYA, J	

ART UNIT	PAPER NUMBER
1655	14

DATE MAILED: 04/03/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/181,585	Applicant(s) Ranum et al
	Examiner Jehanne Souaya	Group Art Unit 1655

☒ Responsive to communication(s) filed on *Nov 20, 2000* .

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-4, 7-19, and 21-51* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☒ Claim(s) *2, 3, 15-17, 19, and 43-48* is/are allowed.

☒ Claim(s) *1, 4, 7-14, 18, 21-42, and 49-51* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☒ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Currently, claims 1-4, 7-19 and 21-51 are pending in the instant application. Finality of the previous office action has been withdrawn, consequently, a new non final action on the merits is set forth below. The amendment filed 11/22/2000 has been entered. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance. Any rejections not reiterated are hereby withdrawn. The following rejections are either newly applied or are reiterated. They constitute the complete set being presently applied to the instant Application.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

New Grounds Of Rejection

Claim Rejections - 35 USC § 112

Enablement

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4, 10,18, and 40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for detecting whether an individual is at risk for developing spinocerebellar ataxia type 8 wherein individuals *at risk* for developing SCA8 have greater than or equal to 80 CTG repeats, does not reasonably provide enablement for determining whether or not an individual has SCA8. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The specification teaches that the ataxias are a clinically and genetically heterogenous group of neurodegenerative disease that are characterized by trinucleotide repeat expansions, the largest group being that of CAG expansions that are translated into polyglutamine tracts (see p. 1, para. 2). The specification also teaches that in general, a high number of CAG repeats in a particular SCA coding sequence indicates that an individual is suffering from spinocerebellar ataxia, or may develop symptoms in the future, and that the number of CAG repeats that is indicative of spinocerebellar ataxia typically varies with the type of SCA (see p. 2, lines 26-30). The specification teaches that an SCA8 allele with less than 80 CTG repeats is normal, and that an SCA8 allele with less than 91, preferably less than 33 combined CTG and CTA repeats is normal (see p 13, lines 14-23).

The specification lacks guidance to enable one skilled in the art to diagnose ataxia type 8 based on the presence of CTG repeat expansions however. The specification teaches a study of kindreds which include family members exhibiting the symptoms of spinocerebellar ataxia (see p.

32). The specification teaches that 25 clinically affected individuals were identified and that subjects that were homozygous for the SCA8 expansion and their heterozygous siblings were affected to a similar degree (see lines 20-25). However, the specification also teaches that 21 individuals who carried the expanded repeat were not clinically affected at the time of evaluation (see lines 28-31). The specification further teaches that unlike other dominant spinocerebellar ataxias, the age of disease onset for SCA8 does not appear to be significantly correlated with the size of the CTG expansion (see p. 34, lines 24-30). The art is silent with regard to diagnosing SCA8 by detecting CTG expansions in the SCA8 allele, therefore the art does not make clear the deficiencies in the specification with regard to *diagnosing* SCA8 solely based on the presence of CTG expansions in the SCA8 allele.

Therefore based on the lack of guidance from the specification and the teaching of unpredictability with regard to *diagnosing* spinocerebellar ataxia type 8 based on the number of repeats, undue experimentation would be required of the skilled artisan to practice the invention as claimed. To be able to diagnose a patient as having spinocerebellar ataxia, the skilled artisan would have to perform a longitudinal kindred analysis, measuring the number of repeats in both affected and unaffected family members, and clinically categorizing each member to determine if an individual who had a large number of repeats actually had or would develop (in the future, hence the need for a longitudinal study) spinocerebellar ataxia. As the specification teaches that unlike other dominant spinocerebellar ataxias, the age of disease onset for SCA8 does not appear to be significantly correlated with the size of the CTG expansion, the skilled artisan would be

required to perform undue experimentation to determine if subjects with a large number of expansions would in fact develop SCA8.

Written Description

4. Claims 1, 4, 7, 9-14, 18, 21-42, 49, 50 and 51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification teaches that the ataxias are a clinically and genetically heterogenous group of neurodegenerative disease that are characterized by trinucleotide repeat expansions, the largest group being that of CAG expansions that are translated into polyglutamine tracts (see p. 1, para. 2). The specification also teaches that in general, a high number of CAG repeats in a particular SCA coding sequence indicates that an individual is suffering from spinocerebellar ataxia, or may develop symptoms in the future, and that the number of CAG repeats that is indicative of spinocerebellar ataxia typically varies with the type of SCA (see p. 2, lines 26-30). The specification teaches that an SCA8 allele with less than 80 CTG repeats is normal, and that an SCA8 allele with less than 91, preferably less than 33 combined CTG and CTA repeats is normal (see p 13, lines 14-23).

With regard to claims 1,7, 9-14, 21-32, 35, 37-39, 41, 42, 49, and 51, (and claims dependent from such) and the recitation of "SCA8 coding sequence", such a recitation reads on the SCA 8 gene, which has not been taught in the specification. The specification defines "coding sequence" to refer to a nucleotide sequence that codes for an mRNA that may or may not be translated into protein. Such a definition reads on a gene, however the specification does not define the gene sequence where the SCA8 allele is located. The specification has only taught a single sequence which is found at the SCA8 allele, SEQ ID NO 1, however, it is unclear if this sequence corresponds to a full length open reading frame as the specification also teaches that the product of the SCA8 mRNA is never encoded into a protein. On page 12, the specification defines SEQ ID NO 1 as genomic DNA that includes the repeat region of SCA8. However a gene includes introns, exons, and regulatory sequences that have not been taught in the specification. The specification has only taught (p 26) that a 1.2 kB insert that contains the CTG expansion and flanking genomic DNA was sequences. The specification does not teach the full sequence, nor does the specification teach whether this insert contained the full length open reading frame of SCA8 or the SCA8 gene. The specification further defines SEQ ID NO 2 as mRNA of the SCA8 coding sequence that contains exons D,C,B, and A. SEQ ID NOS 3 is also defined as mRNA of the SCA8 coding sequence, but SEQ ID NO 3 contains exons E,C,and A. Thus it is unclear what the full length open reading frame of SCA8 is composed of, that is, are SEQ ID NOS 2 and 3 alternative splice variants, or do they only represent partial sequences. Furthermore, if the SCA8 gene is never encoded into a protein, it is unclear whether additional

sequences also comprise the presumed cDNA sequence of SCA8, that is there may be additional exons that are not described in the specification. As the specification does not describe the complete SCA8 region, but only teaches specific SEQ ID NOS that are found within the region, the specification fails to describe a representative number of sequences that are encompasses by the "comprising" language and the "coding sequence" language found in the claims.

With regard to claims 33 and 34, the claims read on sequences that only need have 15 nucleotides from the designated nucleic acid sequences of SEQ ID NO 1. The term "comprising' is considered open language, and reads on any sequence that contains only 15 nucleotides from SEQ ID NO 1 and any number of nucleotides on either side. Such nucleotides could bear little resemblance to the nucleic acid sequence of SEQ ID NO 1. Neither the specification nor the claims set forth any particular structural or functional characteristics that a skilled artisan could use to identify polynucleotides that constitute probes or primers to SCA8 other than those defined by SEQ ID NO. The term "SCA8" is not art recognized other than such a term refers to a particular SCA allele. The term does not make clear the sequence of either the full length ORF of SCA8 or the SCA8 gene, and thus the prior art is silent with respect to structural and functional features that may be used to identify such polynucleotides.

With regard to claims 10, 18, and 40, the specification does not teach diagnosis. The specification teaches a study of kindreds which include family members exhibiting the symptoms of spinocerebellar ataxia (see p. 32). The specification teaches that 25 clinically affected individuals were identified and that subjects that were homozygous for the SCA8 expansion and

their heterozygous siblings were affected to a similar degree (see lines 20-25). However, the specification also teaches that 21 individuals who carried the expanded repeat were not clinically affected at the time of evaluation (see lines 28-31). Furthermore, the specification does not teach predisposition with any SCA8 coding sequence, but with probes and primers to SEQ ID NO 1.

Each of the claimed inventions is a genus for which a representative number of sequences for each genus must be disclosed to meet the written description requirement of 112, first paragraph. As set for the by the Court in *Vas Cath Inc. V. Mahurkar,* 19 USPQ2d 1111, the written description must convey to one of skill in the art "with reasonable clarity" that as of the filing date applicant was in possession of the claimed invention. Absent a written description disclosing a representative number of the species of SCA8 gene, ORF, coding sequences, or sequences "comprising, the specification fails to show that applicant was in fact "in possession of the claimed invention" (with regard to the broad scope of the claims), at the time the application for patent was filed.

Conclusion

5. The following claims are enabled and adequately described by the specification; and free of the prior art: Claims 2-3, 15-17, 19, and 43-48. These claims are drawn to methods and products that indicate a *predisposition* (not diagnosis) to SCA8, and clearly define the region taught in the specification (SEQ ID NO 1), primers and probes that consist of oligonucleotide sequences from this region (SEQ ID NO 1) and the number of CTG and CTA expansions needed to detect a

predisposition to SCA8. Although, the application is not presently in condition for allowance, allowable subject matter does exist. Amendment of the rejected claims to reflect description outlined above, would overcome the rejections presently applied to the instant claims. Applicant's representative is urged to contact the examiner with any questions regarding the new Written Description guidelines and the effect of such on the allowability of the claims.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703)308-6565. The examiner can normally be reached Monday-Thursday from 7:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600

Jehanne Souaya
Jehanne Souaya
Patent examiner
March 19, 2001